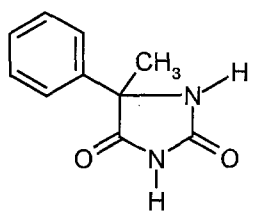
Data Evaluation Report on the aerobic biotransformation of fenamidone metabolite RPA 412636 in aerobic soil

PMRA Submission Number {.....} EPA MRID Number 45385820

Data Requirement: PMRA Data Code:
EPA DP Barcode: D275213
OECD Data Point:
EPA Guideline: 162-1

Test material:
Common name: RPA412636
Chemical name
IUPAC name: (S)-5-methyl-5-phenylimidazolidine-2,4-dione
CAS name: 2,4-Imidazolidinedione, 5-methyl-5-phenyl-(S)-
CAS No: 27539-12-4
Synonyms: S-enantiomer of RPA717879
SMILES string:

Chemical Structure:



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EPA PC Code: 046670

CITATION: Clarke, D.E. 2000. [^{14}C]-RPA 412636: Rate of aerobic degradation in three soil types at 20°C. Unpublished study performed and submitted by Aventis CropScience, Essex, UK. Laboratory Project ID: 17583. Study experimental start date March 30, 1999, and experimental end data June 12, 2000 (p. 39). Final report issued August 22, 2000.

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Regulatory Conclusions: This study, conducted with the major soil metabolite is acceptable. Together with the acceptable 45385819 study conducted with parent fenamidone, it may be used towards satisfying the 162-1 data requirement..

EXECUTIVE SUMMARY

The aerobic soil biotransformation of radiolabeled [phenyl-U-^{14}C]-labeled (S)-5-methyl-5-phenylimidazolidine-2,4-dione (fenamidone metabolite RPA 412636) was studied in a Florida sand soil (pH 7.9, organic carbon 0.7%), a UK clay loam (pH 8.5, organic carbon 2.0%), and a Mississippi silt loam (pH 7.0, organic carbon 0.3%) for 365 days under aerobic conditions in darkness at 20 ± 1°C with a soil moisture of 75% of 1/3 bar. [^{14}C]RPA 412636 was applied at a nominal rate of 0.496 µg a.i./g soil, equivalent to 496 g a.i./ha to all soil types. The experiment was conducted in accordance with the US EPA guideline 162-1 and in compliance with OECD-GLP. The test system consisted of straight-sided glass flasks attached to traps for the collection of CO_2 and volatile organic compounds. Duplicate samples were collected for analysis after 0, 1, 3, 7, 14, 21, 35, 85, 146, 205, 285/287 and 334 (silt loam only), and 365 days of incubation. Soil samples were sequentially extracted with acetonitrile and acetonitrile:water, and by mechanical shaking and Soxhlet extraction. The soil extracts, extracted soil, and volatile trapping solutions were analyzed for total radioactivity using LSC. The extracts were analysed for [^{14}C]RPA412636 and its transformation products by HPLC; peaks were identified by comparison to reference standards. Identifications were confirmed using TLC and LC/MS.

Total recovery of radiolabeled material ranged from 92.48 to 101.51% of the applied amount in the sand soil; 87.65 to 102.88% of the applied amount in the clay loam soil; and 91.66 to 105.37% of the applied amount in the silt loam soil. Corresponding mean recoveries were 97.84 ± 2.50%, 95.71 ± 5.36%, and 97.83 ± 4.76% of the applied amount, respectively. No pattern of decline was observed in the sand and silt loam soil; however, recoveries in the clay loam soil declined from 100.89% at day 0 to 87.65% at day 365.

In the sand soil, the concentration of [^{14}C]RPA412636 decreased from 92.04% of the applied at day 0 to 53.47% at 365 days posttreatment. No major or minor transformation products were identified. Total unidentified radioactivity totaled a maximum 2.05% of the applied. Extractable [^{14}C]residues decreased from 92.04% of the applied at day 0 to 55.52% at 365 days posttreatment. Nonextractable [^{14}C]residues increased from 6.40% of the applied at day 0 to 37.94% at 365 days. Volatile [^{14}C]residues, >90% of which were CO_2, totaled 3.66% of the applied at 365 days posttreatment.

In the clay loam soil, [^{14}C]RPA412636 decreased from 91.58% of the applied at day 0 to 7.63% at 365 days posttreatment. No major or minor transformation products were identified. Unknown 1 (RRT 1.2) was a maximum 4.83% of the applied; other unidentified residues totaled a maximum 2.08%. Extractable [^{14}C]residues decreased from 91.58% of the applied at day 0 to 13.64% at 365 days posttreatment. Nonextractable [^{14}C]residues increased from 9.31% of the applied at day 0 to

38.40% at 365 days. Volatile [^{14}C]residues, >90% of which were CO_2, totaled 35.61% of the applied at 365 days posttreatment.

In the silt loam soil, [^{14}C]RPA 412636 decreased from 94.86% of the applied amount at day 0 to 55.27% of the applied at 365 days posttreatment. No major or minor transformation products were identified. Total unidentified radioactivity totaled a maximum 1.87% of the applied. Extractable [^{14}C]residues decreased from 94.86% of the applied amount at day 0 to 57.14% of the applied at 365 days posttreatment. Nonextractable [^{14}C]residues increased from 2.33% of the applied amount at day 0 to 14.86% of the applied at day 365. Volatile [^{14}C]residues, >90% of which were CO_2, totaled 19.66% of the applied at 365 days posttreatment.

The reviewer-calculated half-lives of [^{14}C]RPA 412636 in sand, clay loam, and silt loam soils were 433.22, 105.02, and 462.10 days, respectively.

A transformation pathway was proposed by the study author. RPA412636 degrades to at least four minor compounds (each <5% of the applied), which in turn degrade to CO_2.

Results Synopsis:

Soil type: Sand
Half-life: 433.22 days ($r^2 = 0.9846$)
Major transformation products: No major transformation products were identified.
Minor transformation products: CO_2

Soil type: Clay loam
Half-life: 105.02 days ($r^2 = 0.9547$)
Major transformation products: CO_2
Minor transformation products: No minor transformation products were identified.

Soil type: Loam
Half-life: 462.10 days ($r^2 = 0.9762$)
Major transformation products: CO_2
Minor transformation products: No minor transformation products were identified.

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I. MATERIALS AND METHODS

GUIDELINE FOLLOWED: This study was reported to have been conducted according to the USEPA Subdivision N Guideline §162-3 (1982) and EU Commission Directive 95/36/EU of 14 July 1995, Annex 1, Section 7.1.1.2, amending Council Directive 91/414/EEC (p. 15). However, Subdivision N Guideline §162-3 concerns anaerobic aquatic metabolism studies. This study was conducted under aerobic conditions in soil moistened to 75% of 1/3 bar (p. 18). Since this study would be considered unacceptable if reviewed under Subdivision N Guideline §162-3 but deviates only slightly from §162-1 (aerobic soil metabolism), the study was reviewed under §162-1.

COMPLIANCE: This study was conducted in compliance with the OECD Principles of Good Laboratory Practice, as set forth by the United Kingdom Department of Health within the Good Laboratory Practice Regulations 1997 (No. 654 Health and Safety). Signed and dated GLP, Quality Assurance, Certificate of Authenticity, and Data Confidentiality statements were provided (pp. 2-5).

A. MATERIALS:

1. Test Material [Phenyl-U-^{14}C]RPA 412636

Chemical Structure:

Description: Solid (p. 16).

Purity: Radiochemical purity: ≥99.8% (pp. 15-16)
Batch No. NXG 3021/1
Analytical purity: Not provided
Specific activity: 4.46 MBq/mg
Location of the radiolabel: Uniformly in the phenyl ring

Storage conditions of test chemicals: Storage conditions were not reported.

Table 1: Physico-chemical properties of RPA 412636.

Parameter	Values	Comments
Molecular weight	190.2 g/mol	
Water solubility	Not reported.	
Vapor pressure/volatility	Not reported.	
UV absorption	Not reported.	
pK_a	Not reported.	
K_{ow}/log K_{ow}	Not reported.	
Stability at room temperature	Not reported.	

Data obtained from Appendix 3, p. 88 of the study report.

2. Soil Characteristics

Table 2: Description of soil collection and storage.

Description	Sand (99/05)	Clay loam (99/07)	Silt loam (99/08)
Geographic location	Citrus Grove, Corkscrew Road, Fort Meyers, Florida	Adisham Court, Adisham, Kent, UK	Delta Research Farm, Leland, Mississippi
Pesticide use history at the collection site	Not provided		
Collection procedures	In accordance with International Standard on Soil Quality.		
Sampling depth (cm)	Not reported.		
Storage conditions	In loosely tied bags the dark at 4°C.		
Storage length[1]	Approximately 1.5-2 months.		
Soil preparation	Sieved 2 mm.		

Data obtained from pp. 16, 18 in the study report.

1 Soils were collected between late January and mid-February. The experimental start date was March 30.

Table 3: Properties of the soils.

Property	Sand (99/05)	Clay loam (99/07)	Silt loam (99/08)
Soil texture[1]	Sand	Clay loam	Silt loam
% sand[1]	96.38	12.22	20.19
% silt[1]	1.83	60.89	73.62
% clay	1.80	26.90	6.19
pH in Water in 1M KCl in 0.01M $CaCl_2$	7.9 7.1 7.7	8.5 7.4 7.0	7.0 6.4 6.1
Organic carbon (%)	0.7	2.0	0.3
Organic matter (%)	1.2	3.4	0.5
CEC (meq/100 g)	9.1	94.8	7.8
Water holding capacity at 1/3 bar (%)	4.0	24.9	11.5
WHC at atmospheric pressure (%)	38.0	67.1	42.3
Bulk density (g/cm^3)	Not reported.		
Soil Taxonomic classification	Not reported.		
Soil Mapping Unit (for EPA)	Not reported.		

Data obtained from Table 1, p. 43 in the study report.

1 Soil textural classes reported to be according to USDA Soil Classification System. These could not be confirmed since sand is defined as particles with diameters between 0.063 and 2 mm and silt as between 0.002 and 0.063 mm. In the USDA system, the boundary between sand and silt is 0.5 mm.

B. EXPERIMENTAL CONDITIONS:

1. Preliminary experiments: No preliminary experiments were conducted.

2. Experimental conditions:

Table 4: Experimental design.

Parameter	Sand (99/05)	Clay loam (99/07)	Silt loam (99/08)
Duration of the test	365 days		
Soil condition: (Air dried/fresh)	Soils were fresh at the start of the study. Soils had to be air-dried for 11-33 days prior to the start of the study to reduce the soil moisture to about 75% of 1/3 bar.		
Soil (g/replicate)	100 g dry weight		

Parameter		Sand (99/05)		Clay loam (99/07)		Silt loam (99/08)	
Test concentrations (mg a.i./kg soil) and equivalent g a.i./ha		0.5 mg a.i./kg soil 512 g a.i./ha		0.5 mg a.i./kg soil 512 g a.i./ha		0.5 mg a.i./kg soil 513 g a.i./ha	
Control conditions, if used		No controls were used.					
No. of Replication	Controls, if used	Four soil samples were left untreated for microbial biomass determination at the end of the study.					
	Treatments	Single samples were collected at each sampling interval.					
Test apparatus (Type/material/volume)		Soils were weighed into straight-sided Erlenmeyer flasks, which were left open to the atmosphere to reduce the moisture content to the target level. The soils were then moistened to 75% of 1/3 bar and allowed to acclimatize at 20 ± 1°C overnight prior to treatment. Following treatment, each flask was placed in a light proof plastic bag and connected to a volatile trapping system. The test apparatus is illustrated on pp. 17-18.					
Details of traps for CO_2 and organic volatile		Humidified CO_2-free air was continuously forced through individual sample flasks, then through two tubes of 2M KOH (30 mL/tube) trapping solutions. At 334 days, (321days for silt loam), the traps were replaced with an ethylene glycol trap, two 2M KOH traps, and a Tenax trap in series.					
If no traps were used, is the system closed/open		Volatile traps were used.					
Co-solvent	Identity	Acetonitrile					
	Final concentration	Approximately 0.1%					
Test material application	Volume of test solution used/treatment	184 µL/treatment		184 µL/treatment		183 µL/treatment	
	Application method	Distributed as evenly as possible over the soil surface. No additional details were provided.					
	Is the co-solvent evaporated?	Yes.					
Microbial biomass of control soil (µg C/g soil; measured by the fumigation extraction method.)		initial	final	initial	final	initial	final
		102	121	284	519	44	57
Microbial biomass/microbial population of treated soil, if provided		initial	final	initial	final	initial	final
		Not provided					

Parameter		Sand (99/05)	Clay loam (99/07)	Silt loam (99/08)
Any indication of the test material adsorbing to the walls of the test apparatus?		Not reported.		
Experimental conditions	Temperature (°C)	20 ± 1°C		
	Moisture content Moisture maintenance method:	75% of 1/3 bar Adjusted with deionized water when needed		
	Continuous darkness (Yes/No):	Yes		
Other details, if any		None.		

Data obtained from pp. 16-19, Table 1, p. 43, in the study report.

3. Aerobic conditions: Sample flasks were continuously flushed with humidified, CO_2-free air (p. 16). No determinations were made to verify that aerobic conditions were maintained.

4. Supplementary experiments: No supplementary experiments were conducted.

5. Sampling:

Table 5: Sampling details.

Parameters	Sand (99/05)	Clay loam (99/07)	Silt loam (99/08)
Sampling intervals	0, 1, 3, 7, 14, 21, 35, 85, 146, 205, 285/287, 334 (clay loam only) and 365 days		
Sampling method for soil samples	Single flasks of each soil type were collected at each sampling interval.		
Method of collection of CO_2 and volatile organic compounds	Trapping solutions were collected and replaced at each sampling interval.		
Sampling intervals/times for: Sterility check, if sterile controls are used: Moisture content: Redox potential/other:	 Sterile controls were not used. At intervals throughout the study (not further defined). Not reported.		
Sample storage before analysis	The first extraction occurred on the day of sampling. Extracts were stored at 4°C in the dark for up to 35 days prior to chromatographic analysis.		
Other observations, if any	None		

Data obtained from pp. 19-20, 32, Tables 2-4, pp. 44-46, in the study report.

C. ANALYTICAL METHODS:

Extraction/clean up/concentration methods: All soil samples were sequentially extracted once with acetonitrile and once or twice with acetonitrile:water (1:1, v:v) using a wrist action shaker (p. 24). Beginning at 3 (clay loam), 7 (silt loam) or 14 days (sand), the soils were further extracted once with acetonitrile:water (1:4, v:v) using a wrist action shaker. After each extraction, the samples were centrifuged and the supernatants decanted and aliquots were analyzed using LSC. Beginning at 14 (clay loam) or 35 (sand and silt loam) days, the extracted soils Soxhlet-extracted with acetonitrile:water (4:1, v:v) for 4 hours (p. 25). The extract was decanted, and an aliquot analyzed using LSC.

The acetonitrile and acetonitrile:water extracts were combined and concentrated using a Turbovap or rotary evaporator (p. 27). The Soxhlet extracts were concentrated using a Turbovap or rotary evaporator. Aliquots of the resulting residues were analyzed by LSC. The remainder was diluted with water analyzed by HPLC (p. 28).

Nonextractable residue determination: Portions of the extracted soils were analyzed for total radioactivity using LSC following combustion (p. 25). The 146-day post-extracted soil was further differentiated into humic acid, fulvic acid, and humin fractions using a 0.5 M NaOH extraction procedure (pp. 26-27).

Volatile residue determination: Aliquots of the trapping solution were analyzed for total radioactivity by LSC (p. 26). The identification of CO_2 was confirmed by barium chloride precipitation; it could not be determined if this was done for each trapping solution or only selected samples.

Total ^{14}C measurement: Total ^{14}C residues were determined by summing the concentration of residues measured in the soil extracts, extracted soil, and volatile trapping solutions (p. 24).

Derivatization method, if used: A derivation method was not employed.

Identification and quantification of parent compound: Extracts were analyzed by reverse-phase HPLC under the following conditions (p. 22): Kromasil 100 5C8 (4.6 x 250 mm, particle size not specified), mobile phase of (A) acetonitrile:water (20:80, v:v) and (B) acetonitrile:water (40:60, v:v) [percent A:B at 0 minutes. 100:0 (%); 5 minutes 100:0 (%); 10 minutes 0:100 (%); 20 minutes 0:100 (%); 25 minutes 100:0 (%); 30 minutes 100:0 (%)], flow rate 1 mL/minute, UV (230 nm) and radioactive flow detection. Column recoveries were 89.9-103.0% of the radioactivity applied to the column (p. 29). RPA412636 was identified by comparison to the retention time of an unlabeled reference standard (p. 28).

To confirm the identify of RPA412636, extracts from 0, 1, 14, 85, 205 and 365 days posttreatment were analyzed by one-dimensional normal phase TLC on silica gel plates developed with methylene chloride:methanol (85:15, v:v; pp. 23, 29). An unlabeled reference compound was cochromatographed with the samples. Radioactive compounds were located by autoradiography, and

unlabeled compounds under UV light. Also, the identification of RPA412636 in the 146-day clay loam extract was confirmed using LC/MS using negative ion electrospray mode (pp. 28, 30).

Identification and quantification of transformation products: Transformation products were separated and quantified as described for the parent.

Detection limits (LOD, LOQ) for the parent compound: Limits of detection for LSC, HPLC, and TLC analyses were not reported.

Detection limits (LOD, LOQ) for transformation products: Limits of detection for LSC, HPLC, and TLC analyses were not reported.

II. RESULTS AND DISCUSSION:

A. TEST CONDITIONS: It was reported that aerobicity, moisture, and other environmental conditions were maintained throughout the study. No supporting records were provided. The study author noted that prior to sampling at day 365, the incubator thermostat malfunctioned for two days and the temperature reached a maximum of 30°C (p. 32). Microbial viability was confirmed at the initiation and termination of the study (Table 1, p. 43).

B. MATERIAL BALANCE: In the sand soil, overall recovery of radiolabeled material averaged 97.84 ± 2.50% of the applied (92.48 to 101.51%; Table 5, p. 47). In the clay loam soil, overall recovery of radiolabeled material averaged 95.71 ± 5.36% of the applied (87.65 to 102.88%; Table 6, p. 48). In the silt loam soil, overall recovery of radiolabeled material averaged 97.83 ± 4.76% of the applied (91.66 to 105.37%; Table 7, p. 49). No pattern of decline in the sand and silt loam soil; however, in the clay loam soil, total [^{14}C]residues declined from 100.89% of the applied at day 0 to 87.65% at 365 days posttreatment.

Table 6: Biotransformation of [^{14}C]RPA 412636, expressed as the percentage of applied radioactivity (mean ± s.d.), in sand soil under aerobic conditions.*

Compound	Sampling times (days)											
	0	1	3	7	14	21	35	85	146	205	285	365
RPA 412636	92.04	93.56	91.22	93.34	93.71	92.64	91.26	85.29	74.17	65.65	56.78	53.47
Unknown 1 (RTT 1.2)	ND	ND	ND	ND	ND	ND	ND	ND	0.76	0.83	1.08	1.90
Unknowns (RTT 0.22, 0.33)	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	0.15	0.15
Total extractable residues	92.04	93.56	91.22	93.34	93.71	92.64	91.26	85.29	74.93	66.48	58.01	55.52
Total volatiles[1]	NA	0.09	0.13	0.18	0.15	0.15	0.25	0.56	1.58	2.15	3.06	3.66
Nonextractable residues	6.40	3.73	6.98	7.99	6.31	8.27	5.76	13.02	19.91	26.59	31.41	37.94
Total % recovery*	98.44	97.38	98.34	101.51	100.17	101.06	97.27	98.86	96.41	95.23	92.48	97.12

* Only a single sample was analyzed at each sampling interval. Data obtained from Table 5, p. 47, and Table 11, p. 51 in the study report.
ND Not detected.
1 No distinction was made between CO_2 and other organic volatiles in the data tables. The study author attributed almost all of the trapped volatiles to CO_2.
NA Not analyzed

Table 7: Biotransformation of [^{14}C]RPA 412636, expressed as percentage of applied radioactivity (mean ± s.d.), in clay loam soil under aerobic conditions.*

Compound	Sampling times (days)												
	0	1	3	7	14	21	35	85	146	272	285	334	365
RPA 412636	91.58	92.86	92.10	90.03	95.66	88.34	82.65	58.75	41.65	30.30	12.33	9.24	7.63
Unknown (RTT 1.2)	ND	ND	ND	ND	ND	ND	ND	2.92	3.52	0.98	4.83	4.24	4.78
Unknown (RTT 0.19)	ND	ND	ND	ND	ND	ND	ND	ND	0.69	ND	0.89	1.97	1.23
Unknowns (RTT 0.22, 0.28)	ND	ND	ND	ND	ND	ND	ND	ND	0.91	ND	ND	0.11	ND
Total extractable residues	91.58	92.86	92.10	90.03	95.66	88.34	82.65	61.67	46.77	31.28	18.05	15.56	13.64
Total volatiles[1]	NA	0.11	0.23	0.37	0.62	0.82	1.94	6.67	14.75	19.84	29.59	33.10	35.61
Nonextractable residues	9.31	6.95	6.14	10.03	6.60	9.84	14.01	26.63	32.21	39.80	40.32	40.15	38.40
Total % recovery*	100.89	99.93	98.47	100.42	102.88	99.00	98.60	94.96	93.73	90.92	87.96	88.81	87.65

* Only a single sample was analyzed at each sampling interval. Data obtained from Table 6, p. 48, and Table 13, p. 53 in the study report.
ND Not detected.
1 No distinction was made between CO_2 and other organic volatiles in the data tables. The study author attributed almost all of the trapped volatiles to CO_2.
NA Not analyzed.

Table 8: Biotransformation of [^{14}C]RPA 412636, expressed as percentage of applied radioactivity (mean ± s.d.), in silt loam soil under aerobic conditions.*

Compound	Sampling times (days)											
	0	1	3	7	14	21	35	85	146	205	287	365
RPA 412636	94.86	100.89	91.82	99.39	95.05	97.96	93.32	86.03	79.17	69.92	65.68	55.27
Unknown (RRT, 1.2)	ND	ND	ND	ND	ND	ND	ND	0.54	ND	ND	1.44	1.87
Total extractable residues	94.86	100.89	91.82	99.39	95.05	97.96	93.32	86.57	79.17	69.92	67.12	57.14
Total volatiles[1]	NA	0.13	0.18	0.14	0.38	0.66	0.85	2.33	5.59	8.29	10.19	19.66
Non-extractable residues	2.33	4.35	5.00	3.33	5.28	6.10	3.93	6.37	11.79	13.81	15.11	14.86
Total % recovery	97.19	105.37	97.00	102.87	100.71	104.72	98.10	95.27	96.55	92.03	92.42	91.66

* Only a single sample was analyzed at each sampling interval. Data obtained from Table 7, p. 49, and Table 15, p. 55, in the study report.
ND Not detected.
1 No distinction was made between CO_2 and other organic volatiles in the data tables. The study author attributed almost all of the trapped volatiles to CO_2.
NA Not analyzed.

C. TRANSFORMATION OF PARENT COMPOUND: RPA412636 degraded most rapidly in the clay loam soil, comprising only 7.63% of the applied at 365 days posttreatment (Table 13, p. 53). In contrast, approximately 54% of the applied RPA412636 remained undegraded in the sand and silt loam soils at 365 days (Table 11, p. 51; Table 15, p. 55).

In the sand soil, [^{14}C]RPA412636 decreased from 92.04% of the applied at day 0 to 53.47% at 365 days posttreatment (Table 11, p. 51). In the clay loam soil, [^{14}C]RPA412636 decreased from 91.58% of the applied at day 0 to 58.75% at 85 days posttreatment, 30.30% at 205 days, and 7.63% at 365 days (Table 13, p. 53). In the silt loam soil, [^{14}C]RPA412636 decreased from 94.86% of the applied at day 0 to 55.27% at 365 days posttreatment (Table 15, p. 55).

Half-life: The half-life of RPA 412636 was determined using linear regression analysis based in first order kinetics as calculated by Excel 2000. The reviewer calculated half-lives were similar to the study author values.

Table 9: Half-life values of RPA 412636 in aerobic soil

Test system	First order linear			DT50 (days)	DT90 (days)
	Half-life (days)	Regression equation	r^2		
Sand	433.22	Linear form y = mx + b as lnC= -kt + lnC_0; lnC_0 is initial concentration (b = y intercept), lnC is concentration at time t (y), k is the slope (m), t is time (x) or kt = lnC_0 - lnC. Half-life (t ½) = -(ln 2/k).	0.9846	472	ND
Clay loam	105.02		0.9547	124	364
Silt loam	462.1		0.9762	461	ND

Data used to calculated the half-life for the entire system obtained from Table 11, p. 51; Table 13, p. 53; and Table 15, p. 55, in the study report. DT50 and DT90 data were calculated by the study author using a nonlinear model (Table 23, p. 60).

TRANSFORMATION PRODUCTS: No transformation products were identified by the study author. In the sand soil, three peaks with Relative Retention Times of 1.2, 0.22, and 0.33 totaled a maximum 2.05% of the applied at 365 days (Table 11, p. 51). In the clay loam soil, one peak (RRT 1.2) was 4.24-4.83% of the applied at 285-365 days (Table 13, p. 53). Three other peaks (RRT 0.19, 0.22, and 0.28) totaled a maximum 2.08% of the applied at 334 days. In the silt loam soil, one peak (RRT 1.2) was a maximum 1.87% of the applied at 365 days (Table 15, p. 55).

NONEXTRACTABLE AND EXTRACTABLE RESIDUES: In the sand soil, extractable [^{14}C]residues decreased from 92.04% of the applied at day 0 to 55.52% at 365 days posttreatment (Table 5, p. 47). Nonextractable [^{14}C]residues increased from 6.40% of the applied at day 0 to 37.94% at 365 days posttreatment. Organic matter fractionation of a 146-day sample indicated that

8.92, 7.30, and 3.69% of the applied was associated with the fulvic acid, humic acid, and humin fractions (Table 9, p. 50).

In the clay loam soil, extractable [^{14}C]residues decreased from 91.58% of the applied at day 0 to 13.64% at 365 days posttreatment (Table 6, p. 48). Nonextractable [^{14}C]residues increased from 9.31% of the applied at day 0 to 38.40% at 365 days posttreatment. Organic matter fractionation of a 146-day sample indicated that 11.52, 4.87, and 15.81% of the applied was associated with the fulvic acid, humic acid, and humin fractions (Table 9, p. 50).

In the silt loam soil, extractable [^{14}C]residues decreased from 94.86% of the applied at day 0 to 57.14% at 365 days posttreatment (Table 7, p. 49). Nonextractable [^{14}C]residues increased from 2.33% of the applied at day 0 to 14.86% at 365 days posttreatment. Organic matter fractionation of a 146-day sample indicated that 5.58, 1.09, and 5.13% of the applied was associated with the fulvic acid, humic acid, and humin fractions (Table 9, p. 50).

VOLATILIZATION: Volatiles totaled 3.66, 35.61, and 19.66% of the applied radioactivity at 365 days in the sand, clay loam, and silt loam soils, respectively (Tables 5-7, pp. 47-49). Volatiles were trapped only in the KOH solution (no quantitative data provided), and using barium chloride precipitation it was shown that $^{14}CO_2$ accounted for 91.61%, 92.81%, and 96.32% of the radioactivity trapped in the KOH solutions from the sand, clay loam and silt loam soils, respectively (sample interval not reported; Table 10, p. 50).

TRANSFORMATION PATHWAY: It was proposed that [^{14}C]RPA 412636 degrades to at least four unknown minor degradates, accounting for <5% of the applied (p. 36). These transformation products in turn are degraded to CO_2.

Table 10: Chemical names and CAS numbers for the transformation products of RPA 412636.

Applicant's Code Name	CAS Number	CAS Chemical Name(s)	Chemical formula	Molecular weight	SMILES string
		No transformation products were identified.			

D. SUPPLEMENTARY STUDY - RESULTS: No supplementary studies were conducted.

III. STUDY DEFICIENCIES: No significant deficiencies that affect the study results were identified. However, it cannot be used to fulfill Subdivision N Guideline 162-1 because it was conducted with a degradate rather than the parent compound. The study does provide supplemental information on a major degradate of fenamidone.

IV. REVIEWER'S COMMENTS:

1. In the document *Reduced Risk Rationale for the Use of Fenamidone on Potatoes and Vegetables* (B0003264, no MRID), it is reported that fenamidone is the S-enantiomer compound with none of the R-enantiomer present (p. 16). It is further stated that analysis demonstrated that all of the metabolites of fenamidone that retain the imidazolinone ring are also pure S-enantiomers. No evidence was provided to support this statement.

   The registrant's code number used in this MRID, RPA412636, does not match the code numbers presented in other MRIDs in this submission. In other MRIDs, the code RPA717879 is used to identify this compound. The reason for the different code numbers was not discussed in any document, but the registrant does note in the *Reduced Risk Rationale* that the racemic mixtures were often referenced in the original study reports. To avoid confusion, the chemical codes used in each study report are used throughout the respective DER.

2. The registrant submitted this study under USEPA Subdivision N Guideline §162-3 (1982). However, Subdivision N Guideline §162-3 concerns anaerobic aquatic metabolism studies. This study was conducted under aerobic conditions in soil moistened to 75% of 1/3 bar. Also, RPA412636 was identified as a major degradate of [C-phenyl-^{14}C]fenamidone in aerobic soil, but only a minor degradate under anaerobic conditions. Therefore, it was assumed that the guideline was misidentified by the registrant and the study was reviewed under the aerobic soil metabolism guidelines.

3. The sand and silt content of the soils reported in this DER are approximate and the soil textural classes could not be confirmed because the reported particle sizes were not distributed according to the USDA Soil Textural Classification System. In the USDA system, the boundary between sand and silt particles is 0.05 mm. In this study, very fine sand is 0.063 - 0.106 mm and coarse silt is 0.020 - 0.063 mm. The study author provided USDA textural classes for the soils, but it was not certain how this was done since the sand/silt distribution was not according to USDA standards.

4. Towards the end of the study, ethylene glycol and a Tenax trap were added to the volatile trapping system because of the evolution of significant amounts of volatile material (p. 17). Quantitative data from these additional traps was not provided; the study author stated that no radioactivity was detected in the additional traps (p. 33).

5. The material balance for the clay loam soil dropped below 90%. The study author attributed the loss to the cumulative loss of a small percentage of CO_2 over the 365-day study (p. 33).

6. The half-lives for the fenamidone in the sand and silt loam soils were extrapolated beyond the termination of the study. The accuracy of the half-life is therefore highly uncertain because it is based on the assumption that the pattern of dissipation remains linear throughout the process.

Microbial degradation typically follows a curvilinear pattern, with the most rapid decline occurring during the first part of the dissipation process.

7. Single replicates were used in the study. Replicate sampling at each sampling interval is preferred, so that normal variability can be quantified and outliers identified.

8. Representative HPLC and TLC chromatograms presented in Figures A5.10-A5.33, pp. 112-135 indicated good separation of peaks.

V. REFERENCES

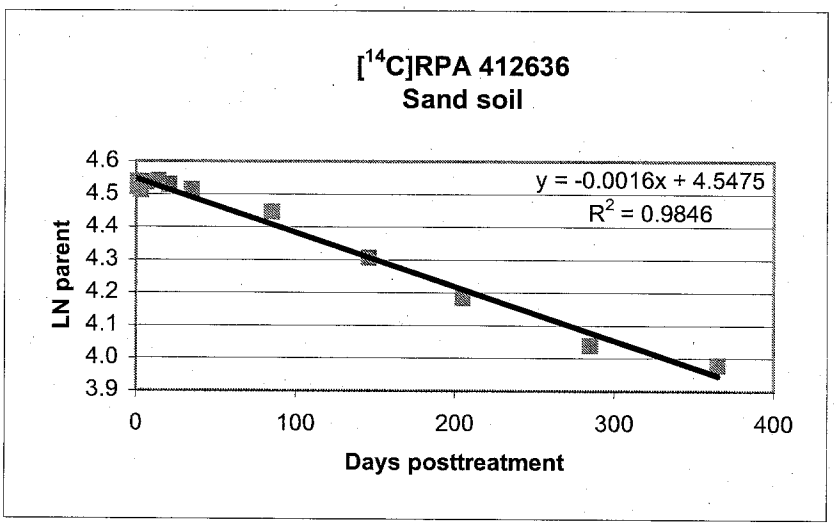
1. Simmonds, M.B., and Burr, C.M. [^{14}C]-RPA 407213 : Rate of aerobic degradation in three soil types at 20°C and one soil type at 10°C, Aventis (formerly RPAL) Document 201610. March 12, 1999.

EPA MRID Number: 45385820
Study Type: Aerobic soil metabolism, 162-1
Test compound: [^{14}C]RPA 412636
Soil: Sand soil

Half-life, days	433.22

Half-life

Days posttreatment	%parent	LN (%parent)
0	92.04	4.5222
1	93.56	4.5386
3	91.22	4.5133
7	93.34	4.5362
14	93.71	4.5402
21	92.64	4.5287
35	91.26	4.5137
85	85.29	4.4461
146	74.17	4.3064
205	65.65	4.1843
285	56.78	4.0392
365	53.47	3.9791



Material balance

Days posttreatment	%applied
0	98.44
1	97.38
3	98.34
7	101.5
14	100.1
21	101.0
35	97.27
85	98.86
146	96.41
205	95.23
285	92.48
365	97.12

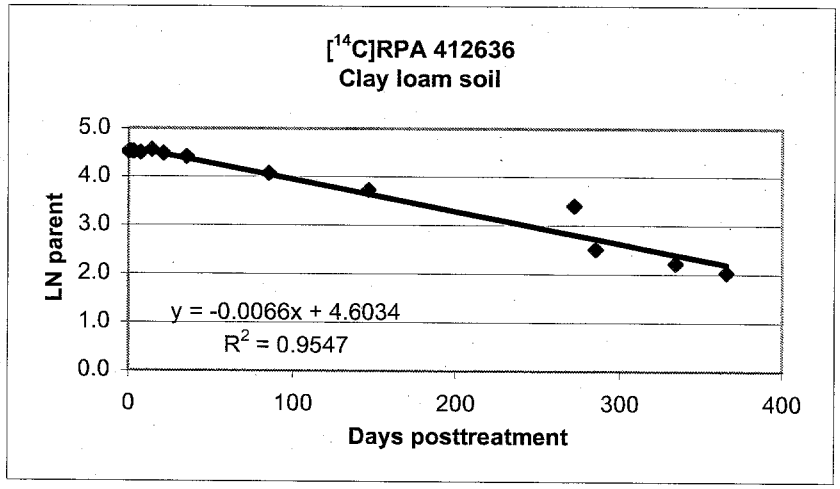
Average	97.84
Standard deviation	2.50

EPA MRID Number: 45385820
Study Type: Aerobic soil metabolism, 162-1
Test compound [^{14}C]RPA 412636
Soil: Clay loam soil

Half-life, days	105.02

Half-life

Days posttreatment	%parent	LN (%parent)
0	91.58	4.5172
1	92.86	4.5311
3	92.10	4.5229
7	90.03	4.5001
14	95.66	4.5608
21	88.34	4.4812
35	82.65	4.4146
85	58.75	4.0733
146	41.65	3.7293
272	30.30	3.4111
285	12.33	2.5120
334	9.24	2.2235
365	7.63	2.0321



Data obtained from DER Table 6

Material balance

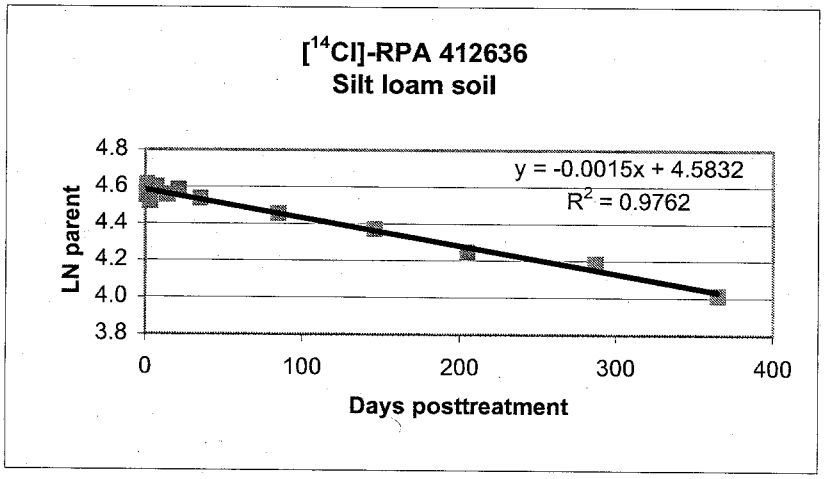
Days posttreatment	%applied
0	100.89
1	99.93
3	98.47
7	100.42
14	102.88
21	99.00
35	98.60
85	94.96
146	93.73
272	90.92
285	87.96
334	88.81
365	87.65
Average	95.71
Standard deviation	5.36

EPA MRID Number: 45385820
Study Type: Aerobic soil metabolism, 162-1
Test compound: [^{14}C]RPA 412636
Soil: Silt loam soil

Half-life, days	462.10

Half-life

Days posttreatment	%parent	LN (%parent)
0	94.86	4.5524
1	100.89	4.6140
3	91.82	4.5198
7	99.39	4.5991
14	95.05	4.5544
21	97.96	4.5846
35	93.32	4.5360
85	86.03	4.4547
146	79.17	4.3716
205	69.92	4.2474
287	65.68	4.1848
365	55.27	4.0122



Data obtained from DER Table 7

Material Balance

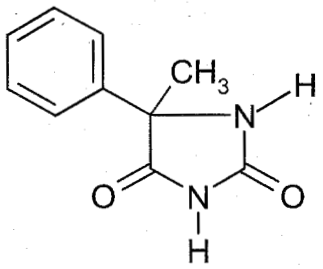
Days posttreatment	%applied
0	97.19
1	105.4
3	97.00
7	102.9
14	100.7
21	104.7
35	98.10
85	95.27
146	96.55
205	92.03
285	92.42
365	91.66

Average	97.83
Standard deviation	4.76

Attachment 2

Structure of Test Substance

RPA 412636
IUPAC name: (*S*)-5-Methyl-5-phenylimidazolidine-2,4-dione
CAS name: 2,4-Imidazolidinedione, 5-methyl-5-phenyl-, (*S*)-
CAS #: 27539-12-4

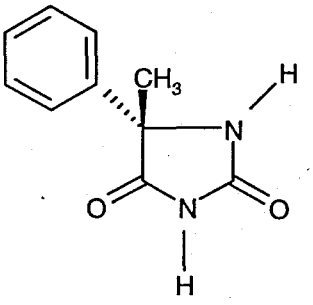


Attachment 3

Transformation Pathway Presented by Registrant
Illustration of Test System

5.4. Proposed Metabolic Pathway

Under aerobic conditions at 20°C in sand, clay loam and silt loam soils RPA 412636 degraded to a series of minor unknown metabolites. This process was accompanied, and followed by, mineralisation to [^{14}C]-labelled carbon dioxide.



RPA 412636

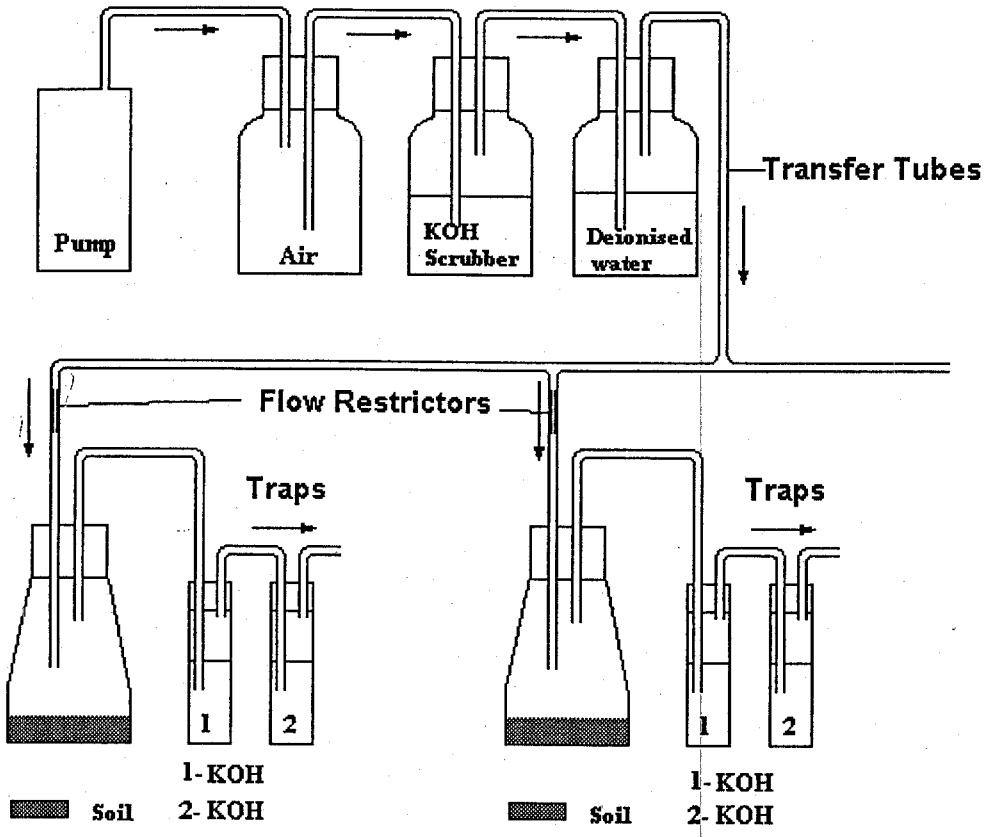
↓

up to four minor unknown metabolites each present at <5% applied radioactivity in any soil type at any timepoint

↓

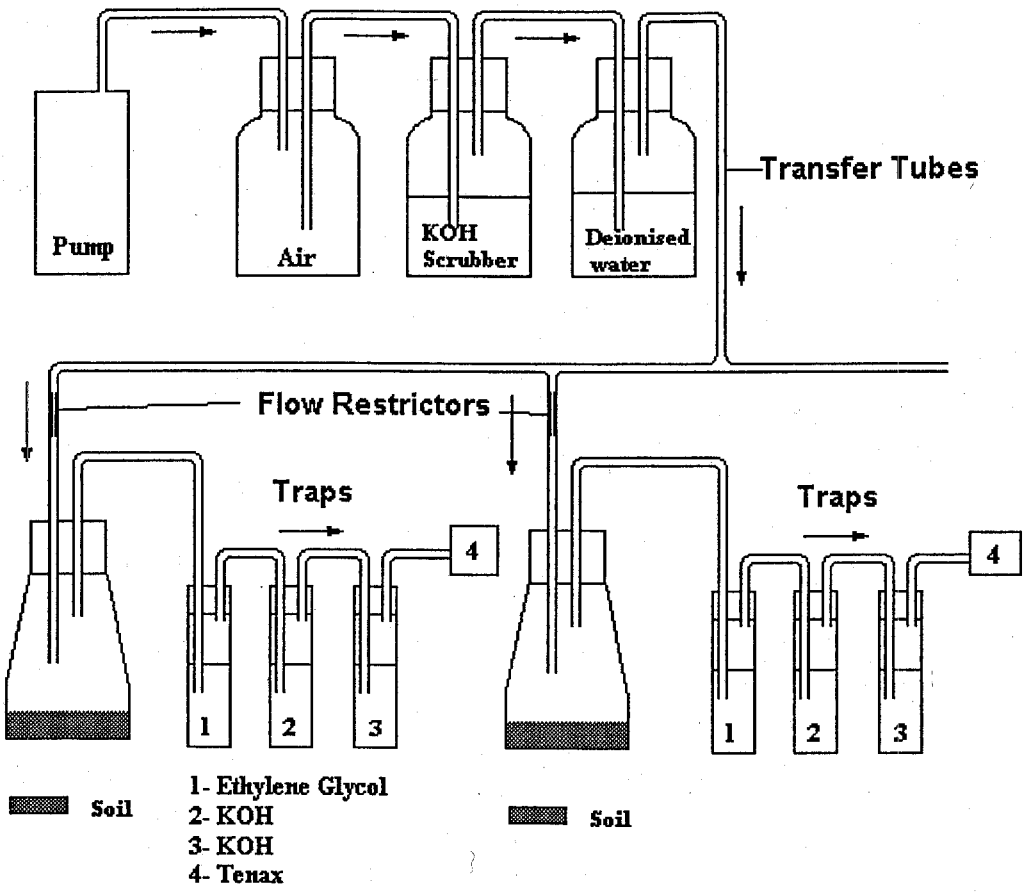
CO_2

Diagram of the Incubation Apparatus



Note : KOH = potassium hydroxide solution

Diagram of the Modified Incubation Apparatus



3.3. Soil Treatment